REMARKS

Applicants request entry of this Amendment and reconsideration of the rejection of the claims.

With entry of this amendment, claims 45, 47-49, 61-63, and 65-67 are pending. With this Amendment, Claims 45, and 47-48 are amended. Support for the amendments to claims can be found throughout the specification, including for example at Figure 2, Figure 4A-E, and supporting description at pages 9-10.

Claims 42-44, 50-53, 55-60, 64, and 68-69 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Petition for Extension of Time

It is noted that a three-month petition for extension of time is necessary to provide for the timeliness of the response. A request for such an extension is made extending the time for response from December 31, 2004 to March 21, 2005.

In the Drawings and Sequence Listing

Replacement sheets and marked-up copies of replacement sheets 5 and 8 are submitted herewith. The appearance of "SEQ ID NO:49" in Figure 7 on Sheet 8 caused the Examiner to issue an objection to the Sequence Listing. "SEQ ID NO:49" is a typographical error and has been corrected to "SEQ ID NO:48." SEQ ID NO:48 properly appears in the Sequence Listing.

The sequences appearing in Figures 4B-4E on Sheet 5 are objected to as being labeled as SEQ ID NO:3, SEQ ID NO: 39, SEQ ID NO:40, or SEQ ID NO:6 but failing to correspond to those sequences in the Sequence Listing. Sheet 5 is amended to indicate that portions of SEQ ID NO:3 and portions of SEQ ID NO:6, are represented in Figures 4B-4E. SEQ ID NO:39 in Figure 4B corresponds to residues 1-101 of SEQ ID NO:39 (shown completely in Figure 4C) and has been so labeled. SEQ ID NO:40 in Figure 4C is now SEQ ID NO: 49. A replacement Sequence Listing is being supplied including SEQ ID NO:49 in Figure 4C.

Applicant's respectfully request acceptance of the Replacement Sheets and Sequence Listing. No new matter is introduced.

In the Specification

The descriptions of the figures are amended at pages 5-6 to conform with the specification description, drawings, and sequence listing. The description for Figure 3 is amended to clarify the relationship between SEQ ID NO:38, shown in the Figure and SEQ ID NO:4. The amendment is supported in the original figure and in the specification at page 9, lines 25-27.

The description for Figures 4B and 4C and other description in the specification identified which regions of SEQ ID NO:3 and SEQ ID NO:6 are represented in Figures 4B and 4C. The sequences for SEQ ID NO:3 and SEQ ID NO:6 presented in the Sequence Listing match the sequences presented in the specification at pages 8 and 9 and match portions displayed in Figures 4B and 4C. The amino acid numbers are corrected in the description of the Figures on page 3 and also described on page 10 to correspond with the sequential residue numbering presented in the Sequence Listing. Correction does not introduce new matter.

The description for Figure 7 now identifies SEQ ID NO:48 as the complementary strand sequence of human EST AA315020 (SEQ ID NO:4). This amendment is supported by Figure 7 as originally filed, the description for human EST AA315020 at page 8, lines 14-24, and further figure description at page 88, lines 15-30.

No new matter is introduced. Entry of the above amendments is respectfully requested.

35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1 – Utility

Claims 42-45, 47-53, and 55-69 are rejected under 35 U.S.C. § 101 as allegedly lacking a specific and substantial utility. These claims are also rejected under 35 U.S.C. § 112,¶1 because the Examiner contends the claimed invention lacks utility. The Office Action alleges that the utilities asserted for SEQ ID NO:3 are not substantial because a specific benefit does not exist and because one would not know if expression of SEQ ID NO:3 would be upregulated, downregulated, or unchanged in cancer. Applicants have cancelled claims 42, 43, 50-53, 55-60, 64, 68 and 69 rendering the rejection of these claims moot. Applicants respectfully traverse these rejections with respect to the remainder of the claims.

Applicants do not have to provide evidence sufficient to establish that an asserted utility is true beyond a reasonable doubt. *In re Irons*, 340 F.2d 974, 978 (CCPA 1965). Nor do Applicants have to provide evidence that establishes the asserted utility as a matter of statistical

certainty. *Nelson v. Bowler*, 626 F.2d 853, 856-867 (CCPA 1980). Rather, Applicants only have the burden of presenting evidence that leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. MPEP § 2107.02 (emphasis in original).

By amending the claims, Applicants do not acquiesce to the rejection. Independent claim 45 is amended into independent form with 47-49 dependent thereon. Independent claim 61 with claims 66 and 67 dependent thereon, and independent claim 62 with claims 63 and 65 dependent thereon are presently pending. Claims 45 and 61 are directed to isolated polypeptides comprising or consisting of the amino acid sequence of SEQ ID NO:3. Claim 62 is directed to an isolated polypeptide consisting of at least 10 amino acids of SEQ ID NO:3.

The utility of the claimed invention is specific, substantial, and credible because the claimed invention is useful for many reasons described in the specification including the detection of misregulation of the Wnt-1 pathway implicated in the transformation of cells into colon, breast, and ovarian cancers. In contrast to the Examiner's assertion, Applicants have shown that a mRNA encoding a polypeptide having SEQ ID NO:3 is over expressed in mammary tumors from Wnt-1 transgenic mice as compared to wild type mice (Example 1, page 87.) SEQ ID NO:3 and its mRNA have demonstrated homology to the human ortholog of SEQ ID NO:6. A human nucleic acid sequence (SEQ ID NO:5) is shown to be upregulated in related human tumors. The correlation between the source of SEQ ID NO:3 and its human ortholog expressed in human cancer cells demonstrates that SEQ ID NO:3 has utility for the detection of transformed cells. (See page 2, lines 14-20; and page 10, line 29 to page 11, line 11). Sufficient nexus is described between SEQ ID NO:3 to a correlated disease condition (i.e. cancer) to provide credible utility.

The Office Action asserts that Haynes (U), Hancock (V) and Allman (W) provide countervailing evidence that shows that one of ordinary skill in the art would have a legitimate basis to doubt the utility of the claimed mouse polypeptide SEQ ID NO:3 based on increased transcript levels for the human polynucleotide SEQ ID NO:5. Applicants respectfully disagree.

As described in the specification for FCTRX polypeptides (e.g., SEQ ID NO:3 and 6), mRNA expression is commonly used to analyze protein activity. Applicants submit it is well known in the art that the primary role of RNA transcripts is to serve as templates for protein synthesis. Haynes, Hancock and Allman provide no teaching to specifically discredit an association between expression of a polynucleotide encoding SEQ ID NO:3 to the expression of

the protein of SEQ ID NO:3, nor expression of SEQ ID NO:5 to the expression of the protein of SEQ ID NO:6.

References cited by the Examiner can also be interpreted as supporting the general correlation between mRNA and protein expression. Haynes is a review article discussing Proteome analysis of expression levels in mid-log yeast. Applicants submit that when the Haynes reference is read as a whole, Haynes states at page 1863, col. 1, "Thus far, we have found a general trend but no strong correlation between protein and transcript levels." (emphasis added) This statement supports an assertion that a correlation between mRNA expression and protein expression is more likely than not true. Similarly, Hancock does not discredit the relationship between mRNA and protein expression. Hancock is lobbying in an editorial note for development of new biomarkers, noting markers generated by proteomics are not always consistent with markers generated from expression profiling. Allman is directed to the BCL-6 expression between two cell populations, germinal center B cells and resting B cells, hence having no relationship to the nucleotides and proteins of the present application and makes no suggestion that of a lack of correlation between mRNA expression and protein expression.

Expression of mRNA and expression of protein are linked. The cited references do not discredit the relationship of SEQ ID NO:3 to its mRNA, nor discredit the relationship of SEQ ID NO:5 to SEQ ID NO:6, nor the relationship between murine and human orthologs. Based on the evidence presented in the specification showing over expression of mRNA encoding SEQ ID NO:3 in mammary tumors from Wnt-1 transgenic mice and over expression of the human ortholog in breast and colonic tumors, it is more likely than not true the over expressed mRNA found in the tumor tissue resulted in corresponding protein expression. Therefore, accepted general trends between mRNA expression and the protein expressed from the mRNA are sufficient to establish utility for the protein of SEQ ID NO:3.

One can make use of SEQ ID NO:3 in a variety of methods, as previously suggested, including: to test potential agents that can, for example, inhibit over-expression of SEQ ID NO:3 in an *in vitro* method or an animal model such as Wnt transgenic mice (p. 46, line 51 and page 68, lines 14-22); or SEQ ID NO:3 can be used to generate antibodies, and those antibodies can be used to detect or treat cancers expressing human orthologs, such as SEQ ID NO:6. Many potential therapeutic agents are first tested in animal models. The Wnt-1 transgenic mouse is such an animal model. Applicants note that the utility guidelines state that "An assay that

measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventative measures or further monitoring. Utility Guidelines ¶6. The specification is sufficient to support these uses and therefore the claimed invention does possess substantial utility.

In light of the specific, substantial and credible utility described above, Applicants respectfully request the rejections under 35 U.S.C. § 101.

The Examiner also rejected claims 42-44, 47-53, and 55-69 under 35 U.S.C. § 112, first paragraph, as lacking written description based upon the contention the specification does not describe any utility for a polypeptide comprising SEQ ID NO:3. Applicants have cancelled claims 42-43, 50-53, 55-60 and 68-69, rendering the rejection of these claims moot. Applicants respectfully traverse the rejection with respect to the remainder of the claims.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added). Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed. Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90, 97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Applicants also submit that the Written Description Guidelines indicate that the written description can be satisfied by a description of the structure, physical and chemical

characteristics and methods of making. Applicants submit that the specification provides written description of the claimed invention.

Applicants have described the sequence of the polypeptide as well as other physical and functional characteristics. Applicants have shown that a polypeptide comprising SEQ ID NO:3 has homology to S100 cytokine family, including the calcium binding domains. See Figure 4B. A mRNA encoding SEQ ID NO:3 was found to be over expressed in mammary tumors from Wnt-1 transgenic mice. (See page 88, lines 1-14). The human homolog of SEQ ID NO:3 has also been found to be over expressed in several types of cancers.

Moreover, as discussed previously, Applicants have described several utilities for this polypeptide including use therapeutically to treat a condition associated with decreased or increased expression of SEQ ID NO:3, such as cancer, immune system disorders, and neurological disorders, as well as in screening assays for identifying agents that bind to a polypeptide comprising SEQ ID NO:3 or that stimulate or inhibit expression of a polypeptide comprising SEQ ID NO:3. (See page 46, lines 1-28). The efficacy of any of these agents for treating or preventing a hyperproliferative disorder can be assayed using in vitro or in vivo assays using animal models (page 70, lines 25-30). One such animal model in the Wnt-1 transgenic mouse, a polypeptide comprising SEQ ID NO:3 is over expressed in mammary tumor cells in Wnt-1 transgenic mice (see example 1) and can be used as a marker to identify and test agents that can affect mammary tumors. In addition, Applicants have described many other utilities for a polypeptide comprising SEQ ID NO:3, including, for example, diagnostic assays. (See page 56 to page 57, line 18).

Thus, Applicants submit the specification as filed provides sufficient description for a polypeptide comprising SEQ ID NO:3 and uses for the polypeptide as claimed. Applicants respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph, rejection on this basis.

35 U.S.C. § 112, ¶1 Written Description and 35 U.S.C. § 112, ¶1 Enablement

Claims 42-44, 47-52, 55-60, 64, 68 and 69 were rejected under 35 U.S.C. 112, ¶l for failing to comply with the written description requirement. The rejection asserted that the claims were directed to a genus of polypeptides having a percentage sequence identity with SEQ ID No:3 and that there is insufficient distinguishing characteristics to identify the genus. Applicants respectfully traverse.

With entry of the present amendment, claims 47-49 are presently pending and rejected under §112¶1. By amending the claims, Applicants do not acquiesce to the rejection. Claims 47-48, as amended, as well as claim 49 are directly or indirectly dependent from claim 45. Claim 45 is directed to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:3. Hence, rejection of claims for failure to comply with the written description requirement is obviated by amendment of claims 47 and 48.

In light of the above comments, Applicants respectfully request withdrawal of the rejection of the claims under the written description requirement.

35 U.S.C. § 112, ¶1 Enablement

The office action rejects claims 42-44, 47-52, 55-60, 64, 68 and 69 under 35 U.S.C. 112, ¶l for failing to comply with the enablement requirement. The rejection is based on a contention the claims are non-enabling because the claims encompass an unreasonable number of inoperative polypeptides, which a skilled artisan would not know how to use. Applicants respectfully traverse.

With entry of the present amendment, claims 47-49 are presently pending and rejected under §112¶1. By amending the claims, Applicants do not acquiesce to the rejection. Claims 47-48, as amended, as well as claim 49 are either directly or indirectly depend from claim 45. Claim 45 is directed to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:3. Hence, rejection of claims 47-49 for lack of enablement is obviated by amendment of claims 47 and 48. Withdrawal of the enablement rejection is respectfully requested.

35 U.S.C. §112 Written Description and Indefiniteness

The Office Action rejects claims 42-44, 47-52, 55-60, 64, 68 and 69 under 35 U.S.C. §112 ¶2 for claiming one or more subgenera of conserved residues or regions. The rejection asserts an issue of new matter. The Office Action rejects claims 42-44, 47-52, 55-60, 64, 68 and 69 as being indefinite for recitation of "the regions corresponding to". Applicants respectfully traverse.

With entry of the present amendment, claims 47-49 are presently pending and rejected under §112 ¶2. By amending the claims, Applicants do not acquiesce to the rejection. Claims 47-49 are directly or indirectly dependent from claim 45 and do not recite "regions

corresponding to". Hence, rejection of claims 47-49 is obviated by amendment of claims 47 and 48. Withdrawal of the rejections under §112 for lack of written description and indefiniteness is respectfully requested.

Interview

Applicants request an interview with the Examiner and his supervisor. Applicants request the Examiner contact Applicants' representative upon receipt of these papers.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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Amendments to the Drawings:

Enclosed herewith are annotated marked-up replacement figure sheets and replacement figure sheets 5 and 8.

ANNOTATED MARKED-UP DRAWINGS

Figure 4B.

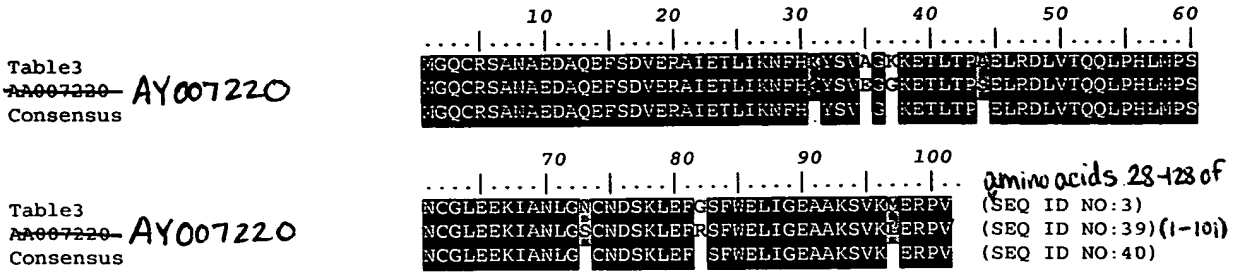


Figure 4C.

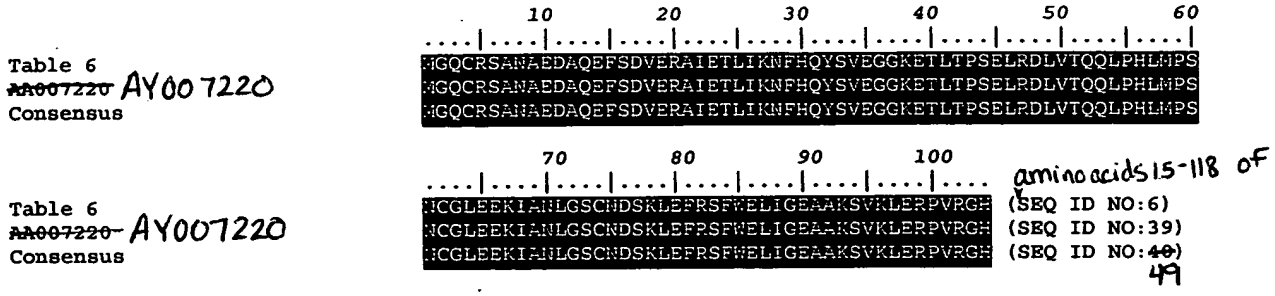


Figure 4D.

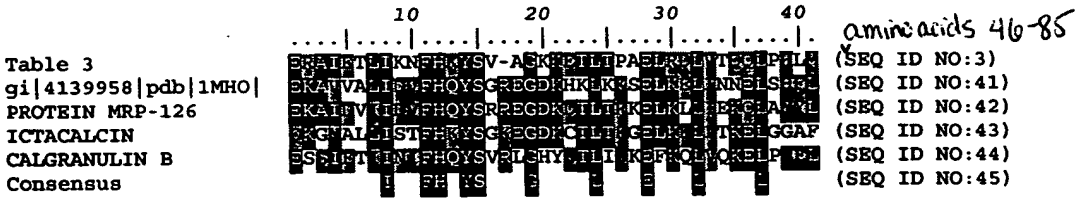
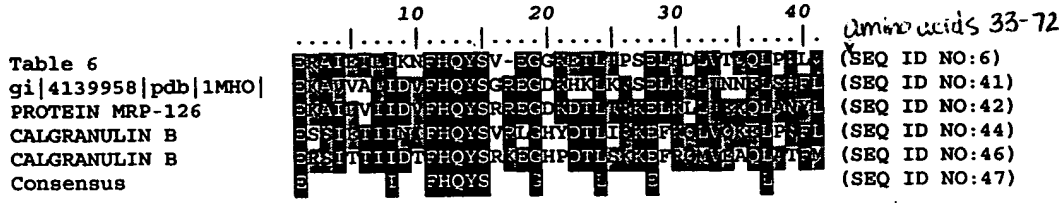


Figure 4E.



ANNOTATED MARKED-UP DRAWINGS

Figure 7 (Table changed from Portrait to Landscape orientation)

********** Contig 1 **********	
	0 8 0 8 0 8 0 8 0 8 0 8
65677221+	GAATTCCAGAGGGAGTTCTCAGTGCCCCCGGACAGGCCTCTCCAGCTTCACACTCTTGGC
AA315020-	TGCCCCCGGACAGTCCTCTCNAGCTTCACACTCTTGGC
consensus	GAATTCCAGAGGGAGTTCTCAGTGCCCCCGGACAGGCCTCTCCAGCTTCACACTCTTGGC
	0 8 0 8 0 8 0 8 0 8 0 8
65677221+	CGCTTCTCCAATCAGCTCCCAGAAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
AA315020-	CGCTTCTCCAATCAGCTCCCAGAAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
consensus	CGCTTCTCCAATCAGCTCCCAGAAACTCCTGAACTCCAGTTTAGAGTCATTGCAGCTGCC
	0 8 0 8 0 8 0 8 0 8 0 8
65677221+	CAGGTTGGCAATTTTCTCTTCCAGGCCACAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
AA315020-	CAGGTTGGCAATTTTCTCTTCCAGGCCANAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
consensus	CAGGTTGGCAATTTTCTCTTCCAGGCCACAGTTGCTCGGCATGAGATGGGGCAGCTGCTG
	0 8 0 8 0 8 0 8 0 8 0 8
65677221+	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
AA315020-	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
consensus	GGTGACCAGGTCCCGTAGCTCAGAAGGGGTCAGCGTCTCCTTCCCACCCTCCACGGAGTA
	0 8 0 8 0 8 0 8 0 8 0 8
65677221+	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTC (SEQ ID NO:37)
AA315020-	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTCCTGAGC
consensus	CTGGTGAAAGTTCTTGATGAGGGTCTCAATGGCCCTCTCCACATCACTGAATTCCTGAGC
	0 8 0 8 0 8 0 8 0 8 0 8
AA315020-	ATCCTCTGCGTTGGCTGACCGACACTGTCCCATGGTGCTCACTGTGTCTGGTCCTTTGGT
consensus	ATCCTCTGCGTTGGCTGACCGACACTGTCCCATGGTGCTCACTGTGTCTGGTCCTTTGGT
	0 8 0 8 0 8 0 8 0 8 0 8
AA315020-	GAGAGTTCTGTTGTCCTAT (SEQ ID NO:~~4~~ 48
consensus	GAGAGTTCTGTTGTCCTAT (SEQ ID NO:5)